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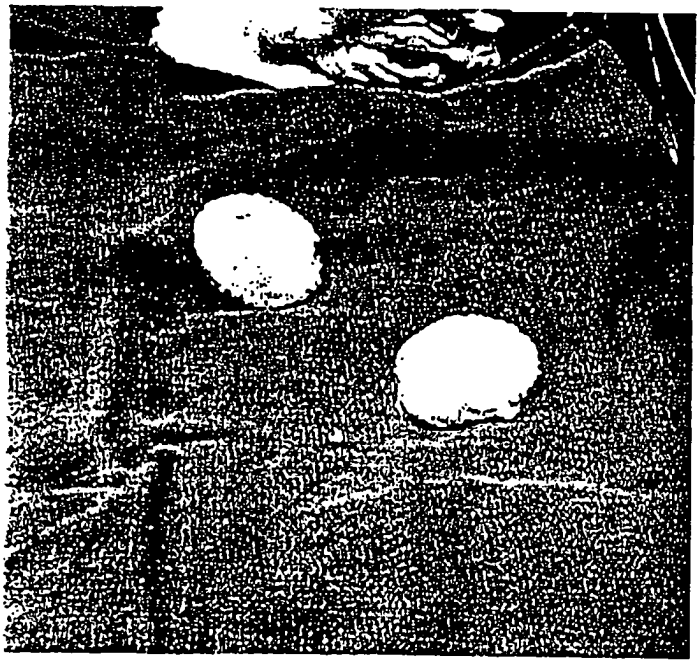
(54) Title: MOLDED IMPLANTS FOR ORTHOPEDIC APPLICATIONS

(57) Abstract

An implant and a method for making and using the implant are disclosed for the repair of bone defects or voids, including defects or voids in the acetabular cup. The implant shapes and compositions of this invention provide advantages not present in impaction grafts and like implants known in the art.



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TITLE OF THE INVENTION

MOLDED IMPLANTS FOR ORTHOPEDIC APPLICATIONS

BACKGROUND OF THE INVENTION

Field of the Invention:

This invention relates to an implant and methods for making and using the implant to fill void defects in bone and to accomplish orthopedic fusions.

Background Information:

In the field of orthopedics, it is desirous to be able to fill bony defects and to be able to fuse joints together using grafting procedures. One procedure that is frequently required is the repair of skeletal void defects. In particular, it is frequently required that bony defects be filled or repaired after trauma or disease has destroyed the native bone. This need may arise from trauma, as in a compound or complex fracture, through removal of diseased tissue, as in, for example, removal of a cancerous growth, or any of a number of other degenerative or damaging conditions. It is common practice in spinal surgery to effect the fusion of adjacent vertebrae by placing bone graft between the vertebrae. This need may arise from a condition such as severe scoliosis, from trauma in which the back is severely damaged, or in the common instance of degenerative disk disease.

Prior to the present invention, the filling of bone defects was usually accomplished through the use of metallic fixation and reinforcement devices or the combination of metallic devices with autograft or allograft.

Recurrent problems in the methods known in the art are the lack of incorporation of the metallic graft materials, the pain associated with autograft harvest, the lack of sufficient amounts of autograft for harvesting, the labor-intensive nature of

autograft and allograft preparation, and the relatively poor performance of commonly acquired allografts.

A recurring problem in the methods known in the art for repairing, for example, the acetabular surface is that frequently, upon insertion into the acetabulum of metallic or polymeric implant materials, voids remain between the back surface of the implant and the pelvic bone remaining in the original femoral socket.

In one method known in the art, generally referred to as "impaction grafting" (see, for example, Elting, et al., Clinical Orthopaedics and Related Research, **319**:159-167, 1995), compressed morselized cancellous allograft bone is used to fashion implants for insertion, for example, into the intramedullary canal of recipients. However, problems associated with that technique include subsidence and the need to use synthetic "glues" such as polymethylmethacrylate. While cortical cancellous chips combined with metallic mesh and circlage wires have been used successfully to fill voids in the acetabulum and proximal femur, and while incorporation of bone chips and *de novo* bone formation at the impaction grafting site has been observed, cortical-cancellous chips handle poorly. The chips tend to bchave like gravel and do not stay in the location into which they are placed unless enclosed by wire mesh or another retaining device. Furthermore, when methyl methacrylate or like cement is pressurized in impaction grafting, large amounts of bone chips become sequestered and therefore are biologically inactive.

In one recent patent, (see US Patent No. 5,824,078 and references cited therein), an apparatus was described for fashioning composite allograft by impaction of cancellous bone and added cement to form acetabular cups. These methods are limited in applicability in that the impacted implant, once formed, is no longer moldable and has limited pliability. The result of such inflexibility is that voids remain, even after the impacted graft is positioned in an appropriate location in a recipient. In addition, the impaction procedure itself requires specialized equipment (such as the rack-and-pinion device to which the 5,824,078 patent is directed) or time consuming in-surgery impaction of bone particles (see the Elting

et al., article, which describes a six-step, *in-situ*, procedure which requires iterative packing and tamping of bone particles).

In US Patent No. 5,439,684, methods of making variously shaped pieces of demineralized swollen bone are disclosed. The shaped bone pieces are composed of large machined pieces of bone of specific shape and are thus not moldable and are not composed of cortical-cancellous bone chips.

This invention provides a solution to the above-noted, long-standing problems by providing specific shapes and compositions of biomaterials for filling of tissue voids, in particular in bony tissue, in an easy to use and effective format.

BRIEF DESCRIPTION OF THE DRAWINGS:

Figure 1 is a representation of a first embodiment of the invention, wherein a disk-shaped bioimplant is provided for insertion into the acetabular socket or other location to fill voids that remain upon insertion of a metallic or other implant.
Figure 2A is a representation of a second embodiment of the invention, wherein a substantially disk-shaped bioimplant is provided, but wherein a sector of the disk-shaped implant has either been removed or has not been included when initially created, so that upon insertion into the acetabluar socket, a substantially cone-shaped or hemisphere-shaped implant, figure 2B, is formed.
Figure 3 provides representations of a number of further embodiments of the invention: Fig. 3A depicts a thin "U"-shaped implant useful in knee revision surgeries; Fig. 3B depicts a thicker "U"-shaped implant useful in spinal fusion procedures; Fig. 3C depicts a thin oval implant useful in knee revision and other surgical procedures; Fig. 3D depicts an implant shape useful in posterior lumbar interbody fusion ("PLIF") procedures; Fig. 3E depicts a dowel shaped implant, useful in spinal and joint fusions; Fig. 3F depicts a tapered dowel shaped implant, useful in spinal and joint fusions.
Figure 4 provides representations of a number of further embodiments of the invention: Fig. 4A depicts a femoral or tibial ring shaped implant useful in interbody fusion procedures; Fig. 4B depicts a round, plug-shaped implant useful

in cranial burr-hole repairs; Fig. 4C depicts a thin "U"-shaped implant which may be folded to provide a cone-shaped or hemisphere-shaped implant depicted in Fig. 4D, useful in knee replacement procedures; Fig. 4E depicts a thin embodiment of the implant depicted according to figure 2, and Fig. 4F depicts the implant when it is folded onto itself to form a cone or hemisphere, useful in acetabular cup reconstruction and other procedures.

Figure 5 provides representations of a number of further embodiments of the invention: Fig. 5A depicts an implant similar to that shown in figures 2 and 4A, except that an asymmetric sector has been removed or excluded from the otherwise circular implant shape; Fig. 5B depicts the implant of Fig. 5A when folded upon itself to form a cone, or hemisphere, useful in acetabular cup and like reconstructions; Fig. 5C depicts a "donut"-shaped implant comprising a flat circular implant having a co-axial void, useful in acetabular cup reconstruction and like procedures where the implant is molded or press-fit to the void space; Fig. 5D depicts a hemi-shell shaped implant which may be press-fit into a bone void, such as in the acetabular cup; Fig. 5E depicts a cone-shaped or hemisphere-shaped implant which may be press-fit into a bone void, such as in the acetabular cup; Fig. 5F depicts a tube which, depending on diameter, may be press-fit or used in an impaction grafting procedure in a bone intramedullary canal; Fig. 5G depicts a nested pair of tubes or cones which may be used for repair of large femoral defects, optionally in association with impaction grafting procedures.

Figure 6 provides representations of a number of further embodiments of the invention: Fig. 6A depicts a sheet while Fig. 6B depicts a strip for repair of traumatic fractures, for cranial and flat-bone repair applications, and for inter-transverse process fusions; Fig. 6C depicts a cord-shaped implant for wrapping or grouting of severe trauma defects, for spinal fusions, inter-transverse process fusions and the like; Fig. 6D depicts a wedge-shaped implant for tibial plateau repairs, joint fusions, and intervertebral body fusions; Figs. 6E, 6F and 7 depict different embodiments of restrictive devices, useful in restricting cement or other flowable materials in plugged intramedullary canals and the like, as in femoral canals during impaction procedures; Fig. 6G depicts an ovoid or football shaped implant useful in repairing cystoid or like bone defects; Fig. 6H depicts a hemi-ovoid or hemi-football shaped implant useful in repairing cystoid or like bone

defects; Fig. 6I depicts a spherical implant useful in repairing cystoid or like bone defects; Fig. 6J depicts a hemi-spherical implant useful in repairing cystoid or like bone defects.

Figure 7 depicts an implant useful as a restrictive device for insertion into a canal, such as the intramedullary canal of a long bone, for example during a cementous impaction procedure.

Figures 8A-C provide X-ray evidence of the efficacy of an acetabular implant according to this invention.

Figures 9A-10 provide photomicrographs of the composition of this invention, before and after implantation.

Figures 10A-D provide further photomicrographs of the composition of this invention, before and after implantation.

Figures 11A-H provides a series of photographs and X-rays showing repair of a severe tibial complex compound fracture after removal of antibiotic loaded methacrylate beads and implantation of the composition according to this invention.

Figure 12A and 12B provide photographs of one embodiment of the implant according to this invention, and its moldability.

SUMMARY OF THE INVENTION:

This invention provides shaped implants and methods for making and using the implants to repair a wide variety of orthopedic defects or lesions, including, for example, acetabular cup damage or repair procedures. The implant may be made from any of a number of known materials, by employing the specific shapes and methods provided herein. Alternatively, specific novel compositions disclosed herein may be used for this purpose. In one embodiment of this invention, the implant is placed in the acetabular socket or other defect requiring repair, and is molded to create a perfect fit between an overlay implant to be inserted into the acetabulum and the bone surface of the pelvis or other overlay implant and basal bony structure.

Accordingly, it is one object of this invention to provide a wide variety of desirably shaped implants for a wide variety of orthopedic applications.

It is another object of this invention to provide implant devices optimized in shape for repair of acetabular cup defects.

It is a further object of this invention to provide a preferred method for making a wide variety of desirably shaped implants useful in a wide variety of orthopedic applications.

It is a further object of this invention to provide a preferred method for repair of acetabular and other orthopedic defects.

It is yet a further object of this invention to provide desirably shaped implants which may be molded to create a perfect fit at the site of implantation.

Other objects and advantages of this invention will become apparent from a review of the complete disclosure and the claims appended to this disclosure.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS:

Any material having the following required characteristics may be employed to produce a device having the shapes and utilities disclosed herein. However, it will be appreciated by those skilled in the art that acceptable implant materials having the shapes and utilities disclosed herein may be prepared even though one or more of the desired characteristics is absent. Essentially, the following list of desirable characteristics would be displayed by an ideal composition, of which certain compositions are disclosed herein:

a. The composition should be bioabsorbable.
b. The composition should be osteogenic.
c. The composition should be osteoinductive.
d. The composition should be osteoconductive.

e. The composition should be malleable or flexible prior to and shortly after implantation so that any desired shape may be produced.

f. The composition should be able to withstand freezing, freeze-drying or other methods of preservation and be able to withstand sterilization.

g. Upon implantation, the materials should fill voids and, if malleable prior to implantation, should then set-up as a hard material in the shape of the voids that have been filled.

Those skilled in the art will appreciate that any autograft, allograft or xenograft material that is molded, machined, cast or otherwise formed into the shapes for use according to this disclosure come within the scope of this invention. However, disclosed herein are specific compositions of preferred characteristics.

Referring now to figure 1, there is provided a representation of a first embodiment **100** of a device that may be prepared and used for acetabular implantation. The device **100** is substantially disk-shaped, having an upper surface **101**, a lower surface **102**, each of which is substantially circular, with a diameter **110**. The diameter **110** is preferably in the range between about 35 and 55 mm, and most preferably is about 45 mm. The disk **100** has a height **120**, which is preferably in the range between about 1 mm and about 10 mm, and is most preferably about 5 mm in height. Furthermore, the disk **100** may be composed of particulate matter **130** embedded or suspended in a base or carrier material **140**. The particulate matter may be collagen sponge, cortical bone chips, cancellous bone chips, cortico-cancellous bone chips, hydroxyapatite or like ceramics, bioactive glass, growth factors, including but not limited to bone morphogenetic protein, PDGF, TGFβ, cartilage-derived morphogenetic proteins (CDMPs), vascular growth factors, and the like, demineralized bone, or any other material considered to be beneficial in the filling of bone or cartilaginous voids and the remodeling thereof into solid, healthy bone or cartilage through the processes of osseointegration (including osteogenesis, osteoinduction, or osteoconduction, as these terms are recognized in the art). The base or carrier material **140** may be any material, which retains a given form upon implantation into the void being filled behind an acetabular implant or in any other orthopedic application. Thus, for example,

fibrin-containing compositions, which coagulate, may be included in the carrier material **140**, as may be various collagen formulations, hydroxylapatite, pleuronic polymers, natural or synthetic polymers, or carboxymethylcellulose, and combinations thereof. Preferably, the carrier material **140** comprises a sufficiently high concentration of gelatin, derived from human or animal tissue, or transgenic sources, such that prior to or upon implantation, the gelatin sets up to form a solid or semi-solid material of the desired shape. Use of gelatin as the base carrier material is considered desirable because, by simply heating a pre-formed device according to any of the embodiments of this invention, the implant device becomes flexible or malleable, and may be caused to precisely fit into the shape of any existing void or defect.

Where gelatin is employed as the base or carrier material, and cortical, cancellous or cortico-cancellous bone chips or demineralized bone is included in the carrier, the following percentages, on a weight basis, are considered desirable for formation of the variously shaped implants disclosed herein: the gelatin is preferably present at between about 12 to 27 weight percent. Demineralized bone is preferably present at between about 15 to 33 weight percent. Finally, cancellous bone chips, cortical bone chips or cortico-cancellous bone chips are preferably present at between about 70 to 100 volume percent. The bone chips soak up the gelatin/demincralized bone material so that approximately equal volumes of the gelatin/demineralized bone and bone chips are preferably combined to produce the final preferred composition. Devices formed from this composition meet all of the requirements of a desirable implant material set forth above. Naturally, those skilled in the art will appreciate that a wide variety of supplemental constituents may be included in the composition. Thus, for example, growth factors, antibiotics, anti-inflammatory or other biologically active agents may be included at percentages that may be defined through routine experimentation, so long as the basic properties of the implant material is not adversely affected.

Using the appropriate concentration of gelatin, demineralized bone (to provide osteogenic factors) and cortical-cancellous bone chips (to provide structural

strength and bone void filling capacity), a composition that is malleable above body temperature may be produced. Upon implantation or upon cooling, a solid device forms which may be machined or warmed for molding into any desired shape.

Referring now to figure 2A, there is shown a further embodiment **200** of the device according to this invention. This device is similar to that shown in figure 1, in that it has an upper surface **201**, a lower surface **202**, both of which are substantially circular. However, from this embodiment of the invention, a sector **203** has been removed or has not been included in the formation of the device, resulting in what will be referred to herein as a "filled-C-shape". The purpose of this design modification is discussed in connection with the description of figure 2B below. The composition of the device shown in figure 2A and that of figure 1 may be similar, as are its desirable characteristics. The diameter **210** of the device **200** is preferably between about 50 mm and about 150 mm, and is most preferably between about 75 mm and 90 mm. The height **220** of the device is between about 1 mm and about 10 mm, and is most preferably about 5 mm. In addition, the particulate materials **230,** when included, are similar to the particulate materials **130**. The base or carrier material **240** is likewise similar to the carrier or base material **140**. The angle formed between the adjacent sides **204** and **205** of the device **200** that exist by virtue of the absent sector **203** may be any angle greater than zero degrees and less than three-hundred and sixty degrees, and is preferably between about 90 and 150 degrees, and is most preferably about 120 degrees.

In figure 2B, there is shown the device **200**, wherein the adjacent sides **204** and **205** have been brought into contact, to form a substantially cone-shaped or hemisphere-shaped implant **260**. Desirably, the device retains thermoplastic behavior for a limited amount of time after formation, so that the desired shape may be formed from the cone-shaped implant **260**.

Based on the foregoing disclosure, it will be apparent to one skilled in the art that a wide variety of shapes and orthopedic applications may be addressed according

to this invention. As examples of the wide-variety of applications and shapes that may be addressed by this invention, reference is made to figures 3 through 7 included with this disclosure. Thus, Figure 3 provides representations of a number of further embodiments of the invention: Fig. 3A depicts a thin "U"-shaped implant **300** useful in knee revision surgeries. Fig. 3B depicts a thicker "U"-shaped implant **310** useful in spinal fusion procedures. Fig. 3C depicts a thin oval implant **320** useful in knee revision and other surgical procedures. Fig. 3D depicts an implant shape **330** useful in posterior lumbar interbody fusion ("PLIF") procedures. Fig. 3E depicts a dowel shaped implant **340**, useful in spinal and joint fusions. Fig. 3F depicts a tapered dowel shaped implant **350**, useful in spinal and joint fusions. According to the methods disclosed above, various percentages of particulate materials may be included in each of these disclosed shapes, as defined by routine experimentation, for particular applications. In addition, methods for conducting posterior lumbar interbody fusions, spinal fusions induced by dowels and the like may be carried out according to methods known in the art, but using the novel devices disclosed herein.

Further examples of implant shapes that may be produced and used according to the present disclosure are depicted in Figure 4. Thus, Fig. 4A depicts a femoral or tibial ring shaped implant **400** useful in interbody fusion procedures. Fig. 4B depicts a round, plug-shaped implant **410** useful in cranial burr-hole repairs. Fig. 4C depicts a thin "U"-shaped implant **420** which may be folded to provide a cone-shaped or hemisphere-shaped implant **430** depicted in Fig. 4D, useful in knee replacement procedures. Fig. 4E depicts a thin embodiment **440** of the implant depicted according to figure 2, and Fig. 4F depicts the implant **450** when it is folded onto itself to form a cone, or hemisphere, useful in acetabular cup reconstruction and other procedures.

Additional examples of implant shapes that may be produced and used according to the present disclosure are depicted in Figure 5. Thus, Fig. 5A depicts an implant **510** similar to that shown in figures 2 and 4A, except that an asymmetric sector **511** has been removed or excluded from the otherwise circular implant shape. Fig. 5B depicts the implant of Fig. 5A when folded upon itself to form a

cone or hemisphere **520**, useful in acetabular cup and like reconstructions. Fig. 5C depicts a "donut"-shaped implant **530** comprising a flat circular implant having a co-axial void, useful in acetabular cup reconstruction and like procedures where the implant is molded or press-fit to the void space. Fig. 5D depicts a hemi-shell shaped implant **540** which may be press-fit into a bone void, such as in the acetabular cup. Fig. 5E depicts a cone-shaped or hemisphere-shaped implant **550**, which may be press-fit into a bone void, such as in the acetabular cup. Fig. 5F depicts a tube **560** which, depending on diameter, may be press-fit or used in an impaction grafting procedure in a bone intramedullary canal. Fig. 5G depicts a nested pair of tubes or cones **570**, which may be used for repair of large femoral defects, optionally in association with impaction grafting procedures. Each of these shapes may be fashioned by hand, molded, extruded or formed by other means known in the art. In addition, solid materials may be machined to produce the desired shapes, or because of the thermoplastic properties of gelatin, the desired shapes may be produced by known stereolithographic processes.

Yet further examples of the shapes that may be produced and used according to this invention are depicted in Figure 6. Thus, Fig. 6A depicts a sheet **600** while Fig. 6B depicts a strip **610** for repair of traumatic fractures, for cranial and flat-bone repair applications, and for inter-transverse process fusions. Fig. 6C depicts a cord-shaped implant **620** for wrapping or grouting of severe trauma defects, for spinal fusions, inter-transverse process fusions and the like. Fig. 6D depicts a wedge-shaped implant **630** for tibial plateau repairs, joint fusions, and intervertebral body fusions; Figs. 6E, 6F and 7 depict different embodiments of restrictive devices, **640**, **650**, **700**, useful in restricting cement or other flowable materials in plugged intramedullary canals and the like, as in femoral canals during impaction procedures. The flow restrictor **640** has a classic "cork" stopper shape. The implant **650** has a tapered shape like that of the "cork" **640**, but the device **650** is formed by a plurality of stacked "ribs" **651-655** of decreasing diameter. Naturally, the ribs may be formed by molding, such that separate elements **651-655** need to be separately produced. The implant **700** comprises an upper, solid portion **710** having a substantially "cork" shaped configuration. Affixed at seam **720** to the upper solid portion **710** is a thin, hollow, lower portion

730. The thin lower portion **730** folds upward about seam **720** upon insertion of the implant **700** into a lumen **780** of a bone **790** to form a tight seal **740** surrounding the upper plug portion **710**. Fig. 6G depicts an ovoid or football shaped implant **660** useful in repairing cystoid or like bone defects. Fig. 6H depicts a hemi-ovoid or hemi-football shaped implant **670** useful in repairing cystoid or like bone defects. Fig. 6I depicts a spherical implant **680** useful in repairing cystoid or like bone defects. Fig. 6J depicts a hemi-spherical implant **690** useful in repairing cystoid or like bone defects.

Having generally described the invention, including the best mode and preferred embodiments thereof, the following section provides specific exemplary support for the invention as disclosed and claimed. However, the specifics of these examples are not to be considered as limiting on the general aspects of this invention as disclosed and claimed.

Example 1: REPAIR OF AN ACETABULAR CUP DEFECT:

A patient presents with a severe osteolytic lesion behind a primary acetabular implant, due to wear-debris induced osteolysis. In this case, a revision surgery was indicated to replace the worn acetabular component and to remove the lesion. After removing the original acetabular component, the bone lesion was curetted out leaving a healthy bleeding bone mass. A cone- or hemisphere-shaped device was made from 100% v/v cortical-cancellous chips mixed with 68% v/v demineralized bone matrix in a gelatin carrier (24% w/w demineralized bone matrix, 26% w/w gelatin, 50% w/w water) was heated to soften the implant, which was then folded to form a cone or hemisphere. This softened cone or hemisphere of allograft was then forced into the curetted lesion and compressed with the fingers or a trial acetabular cup. A trial cup or a reamer was used to shape the allograft into the form of the back of the new acetabular component. Once the material hardened, the new acctabular component was placed on top of the allograft cup and screwed into place. The resulting efficacy is plainly evident in a series of X-rays of a patient that underwent this procedure. See figure 8.

Figure 8A shows the pre-operative condition of an implant in which the osteolytic defect surrounding the implant articulating surface is clearly evident as the absence of bone mass in the X-ray. Figure 8B shows an immediate post-operative X-ray, showing the implant with the above-described composition located where the osteolytic defect existed. Figure 8C shows the same patient six months after completion of the osteolytic defect repair operation. Growth of new bone and repair of the defect is clearly evident.

Example 2: PLACEMENT OF A PRIMARY HIP ACETABULAR CUP:

Press-fit implants are used in younger patients because the long-term success of these implants is improved over those that are cemented into place using methacrylate bone cement. The reason for this improved long-term success is that the bone directly bonds to the surface of the implant. Because bone-to-implant bonding is improved by the incorporation of a porous coat in the implant, most press-fit orthopedic implants now have a porous coating. However, even with a porous coating, after explantation, most implants are found to only have bonded to the bone over approximately 20% of the surface area. Research has also shown that the long-term success of the implant is roughly correlated with degree of host-implant bonding. The degree of host-implant bonding is severely affected by the quality of the fit between the bone and the implant. If there is too much play in the bone-implant fit, then little or no bonding occurs and it will be necessary to cement the implant into place. By contrast, the osteoinductive, osteoconductive or osteogenic matrix according to this invention, which closely and concurrently interdigitates with both the porous surface of the implant and the bone into which the implant is inserted, facilitates repair of even poorly cut cavities in bone for press-fit insertion of implants. Interdigitation between the porous implant surface and bone causes bone to be induced or conducted from the bleeding bone into the porous coating and thereby induce much better bone-implant bonding. Bearing these considerations in mind, a young, otherwise healthy, patient presenting with osteoarthritis of the hip is treated as follows: It is noted that the degree of advancement of osteoarthritic bone destruction is such that drug-therapy is insufficient to relieve pain and the patient has limited mobility. In this case, a primary press-fit hip replacement is indicated. Through standard surgical

techniques, the natural hip is removed and prepared for replacement with a metallic hip. The acetabulum is prepared by carefully reaming out a space that fits to the back of the acetabulum. A doughnut-shaped acetabular implant (Fig. 4A or 5C) is prepared by warming in a water bath. The warm doughnut-shaped implant is placed into the patient's prepared acetabulum. While the doughnut-shaped implant is still warm, the porous acetabular cup is placed on top of the doughnut-shaped implant and is hammered into place. The particle size and viscosity of the doughnut-shaped implant material allows the material to easily flow into the porous coating of the implant and into the host's cancellous bone.

Figure 9A shows a photomicrograph (40-X) of stained (H&E) composition according to this invention. Based on the staining, the different components of this composition are identified. Note the preferred relative uniformity, preferably between about 125 μm to about 5mm, and preferably, between about 500 μm to about 1 mm or between about 1mm to about 3.35 mm. We have found that bone chips uniformly formed within these preferred size ranges result in surprisingly improved induction and conduction of new bone formation and improved handling of the composition. In figure 9B, the same material is viewed under higher magnification (100X), showing the interpenetration of gelatin into and onto the cortical-cancellous chips and demineralized bone matrix of the composition. Figure 9C shows a biopsy after implantation of this composition in a human female, 6 months after implantation, showing new bone formed onto the surface of a piece of allograft (H&E, 100X). Noticeable are the numerous cutting cones within the mineralized allograft, indicating that the allograft bone will continue to be fully remodeled over time. Figure 9D shows a biopsy of new woven bone between mineralized allograft chips (H&E, 100X). It should be noted that the area between the spicules would normally be filled with healthy marrow. However, in this case, it can be seen that these areas are filled with fibrous inflammatory tissue cause by wear debris from a failed prosthesis. Figure 10A shows additional photomicrographs of a biopsy from a human female six months after implantation of the composition of this invention. This photograph shows details of a cutting cone in a piece of mineralized allograft (H&E, 400X), revealing the presence of osteoclasts, osteoblasts and a cement line, whereby implant material is remodeled

into normal healthy recipient bone. Figure 10B shows a detailed photomicrograph of a cement line between mineralized allograft and new bone (H&E, 400X), revealing osteoblasts at the periphery of the allograft. Figure 10C is a photomicrograph of normal marrow found in areas adjacent newly formed bone, unaffected by wear debris (H&E, 400X). Figure 10D provides a detail of the filamentous wear debris found in the fibrous inflammatory tissue (H&E, 400X).

These photomicrographs clearly demonstrate that the composition of this invention, whether provided in a pre-formed shape, or molded to fit precisely into a recipient implant site, results in rapid remodeling and osteoinductive and osteoconductive effects. Accordingly, gaps that might otherwise prevent new bone formation and ingrowth may be filled with the composition of this invention to induce union between bone and implant materials. Thus, in one specific embodiment of this invention, a porous implant or an implant having a porous coating is contacted with the composition according to this invention. For example, in a total knee arthroplasty, typically an implant having 500-700 μm metal beads contacted with the sawn-off end of the femur. By application of the composition of this invention at the union surface, rapid ingrowth of bone into the metal bead interstices is induced by driving the implant surface into a pre-formed or molded shape formed from the composition according to this invention.

Example 3: REPAIR OF A COMPLEX COMPRESSION FRACTURE:

Complex compression fractures are frequently associated with significant bone loss because the nature of the fracture is such that the bone is shattered and many of the bone fragments are irretrievable. Current practice dictates the collection of as many bone pieces as possible and the placement of those pieces back into the fracture site. Missing pieces are normally replaced with morselized autograft taken from the hip, from the rib, or from the fibula. Occasionally, artificial grafting materials are used with limited success. Allografts have also been used, with varying success, largely dependent upon the nature of the allograft and its source. The application of malleable or moldable pre-formed and appropriately-shaped implants to this type of repair allows the surgeon to effectively replace the

lost bone, without inducing additional trauma by harvesting autograft from another surgical site.

Accordingly, a complex fracture, such as one in the radius, is repaired by following standard surgical techniques to clean the fracture site followed by placement within the fracture of malleable allograft implant material of this invention in the form of a football, sphere, hemi-football, hemisphere, or sheet/strip. Shattered bone particles are packed around the malleable material. Alternatively, the shattered particles of bone are placed into the fracture site and then strips or cords of malleable implant material according to this invention are laid over the fracture site. Malleable cord-shaped implant material of this invention is optionally used as an adjunct or in place of circlage wires to fix the fracture fragments into place.

Figure 11 shows a surgical procedure in a tibia of a patient who experienced a complex compound fracture into which, for a period of four weeks, had been implanted gentamycin impregnated polymethylmethacrylate "beads on a string". Figure 11A shows circular structures in the center of the photograph which are the beads, implanted in an effort to treat a local infection at a fracture site. Figure 11B shows a pre-operative X-ray of the surgical set-up, again with the implanted beads visible in the bone void. Figure 11C shows the intra-operative procedure whereby the implanted beads were removed. Figure 11D shows the large cavity remaining after removal of the beads. Figure 11E shows a photograph of the composition according to this invention, formed in the shape of two dry eight cubic centimeter disks, prior to implantation. Figure 11F is an intra-operative photograph, after implantation of sixteen cubic centimeters of the composition of this invention. The implant material is clearly visible, and as can be seen from this photograph, is moistened by body fluids, but is not soluble and is not washed away. Figure 11G shows the implant site immediately post-implantation. The site of the implant within the void can be discerned as a faint cloud within the void. Figure 11H is an X-ray photograph of the implant site six-weeks post implantation. It can clearly be seen that the implant material has remodeled to

form solid bone mass, while a portion of the void into which implant material was not or could not be implanted remains a void.

Example 4: REPAIR OF OSTEOLYTIC CYSTS:

Osteolytic cysts and other growths on bone that must be removed are typically difficult to replace. Traditional practice dictates that large cystic defects be filled with weight- bearing allograft or autograft. Alternative techniques have employed synthetic materials with limited success.

In this application of the malleable implant material of this invention, cystic defects are repaired after removal of the cyst by placing warm, malleable implant material according to this invention onto the defect and forming it to completely fill the void. The material according to a preferred embodiment of this invention remodels into natural bone in a period ranging from between about 6 weeks to about 9 months.

Example 5: INTERTRANSVERSE PROCESS SPINAL FUSION:

Intertransverse process spinal fusion is generally accomplished by the joint application of both metallic fixation devices and the use of autograft, which is generally harvested from the patient's hip. The autograft harvest is associated with a high rate of morbidity (21%). The use of a grafting material that is effective without the necessity of harvesting autograft would greatly benefit patients in need of such procedures.

Accordingly, after standard surgical preparation including rigorous decortication of the transverse processes and the facets of two adjoining vertebrae, a malleable pre-molded form (strips or cords) of the malleable implant material of this invention are lain gutter alongside the vertebral bodies. Local bone reamings are optionally mixed or intermingled with the still warm and malleable implant material and then the implant material is pressed into the bleeding bone bed.

Example 6: FILLING OF CRANIAL BURR HOLES:

Cranial burr-holes are created whenever it is necessary to cut into the skull in order to gain access to the brain. Current technique dictates the use of plaster of paris-like substances, metallic meshes, and bone waxes to fill these holes, or to not fill them at all. None of the commonly employed products and procedures induce bone to grow across the defect, and some of these products and procedures actually inhibit the growth of the bone.

Accordingly, in this application, a disk-shaped piece of pre-molded implant material according to this invention is placed, warm, into the burr-hole defect, with a small lip of the implant material remaining above the surface to serve as a temporary support for the material. It is anticipated that the temporary support is unnecessary after a period of several days, after which the plug is expected to remain in place on its own. It is anticipated that new bone grows into the remaining gap to completely bridge the gap within about 6 weeks to about 9 months.

Example 7: MOLDING OF THE COMPOSITION OF THIS INVENTION:

Figure 12 shows the formability and moldability of the composition of this invention. Figure 12A shows a dry cone or hemisphere of the composition. Upon hydration and heating to about 43 to about 49 degrees centigrade, the material becomes moldable, and re-sets at body temperature, as shown in figure 12B, where the moldable material is being press-fit by finger pressure into a cavity. Once set-up, the material is easily reamed or drilled for placement of any desired prosthesis.

Example 8: PRODUCTION OF CORTICAL, CANCELLOUS OR CORTICAL-CANCELLOUS BONE CHIPS FOR INCLUSION IN THE COMPOSITION OF THIS INVENTION:

Corticocancellous chips were processed from allograft obtained from the iliac crest, iliac crest segments and from metaphyseal cancellous bone. When metaphyseal ends and iliac crests are used, an approximate mixture of 20%:80% to about 50%:50% cortical:cancellous bone chips is obtained. The bone chips are produced after debridement and antimicrobial treatment in a class 10 or class 100 cleanroom. Appropriately cleaned and sectioned bone was ground in a bone mill fitted with a sieve, to ensure that all collected bone chips are of a fairly uniform size between about 125 μm and about 5 mm. Preferably, the collected bone chips are in the size range of about 125 μm to about 1 mm or between about 1 mm and 3.35 mm. The ground bone chips were soaked in peroxide, with sonic treatment. The peroxide treatment was repeated until no more fat or blood was visible, the peroxide was decanted and the chips were soaked in povidone iodine solution. The chips were then rinsed with water, and then soaked in an ascorbic acid solution, followed by treatment with isopropanol, with sonic treatment. Finally, the chips were treated with a further peroxide soak, followed by a water rinse, and then lyophilization. The dried chips were then sieved to select the desired size range of bone chips desired. Samples were cultured to ensure sterility.

Example 9: PREPARATION OF THE COMPOSITION OF THIS INVENTION FOR MOLDING INTO DESIRED SHAPES:

A known weight of ground lyophilized gelatin of up to 850μm particle size was mixed with a known weight of demineralized bone particles of between about 250μm and 850μm. A known weight of water was added to the combined gelatin and demineralized bone, and thoroughly mixed. The gelatin, water, demineralized bone composition was then warmed to form a paste of known volume, and a fifty-percent to 100 percent volume of corticocancellous bone chips of between about 125μm and 5 mm particle size was then added and the entire composition was thoroughly mixed, with repeated warming steps as needed to ensure thorough

mixing. The mixed composition was then molded into desired shapes, which are stored in sealed sterile pouches or like containers. Upon use, a surgeon uses the shaped material in its prc-formed shape, or warms the material until it becomes moldable, before implanting the material into a desired implant site.

WHAT IS CLAIMED IS:

1. An implant for repair of bone voids or defects, wherein said implant exhibits the following characteristics:
   a. the implant composition is bioabsorbable;
   b. the implant composition is osteogenic;
   c. the implant composition is osteoinductive;
   d. the implant composition is osteoconductive;
   e. the implant composition is malleable prior to and shortly after implantation so that any desired shape may be produced to exactly conform to the shape of the implant site; and
   f. the implant composition is able to withstand freezing, freeze-drying, and sterilization.

2. The implant according to claim 1 wherein said implant is implanted in the form of a pre-formed shape, or is molded to form a new shape or is molded *in-situ* upon implantation, to fill voids, such that said implant sets-up as a hard material in the shape of the voids that have been filled.

3. The implant according to claim 2 comprising a base or carrier material which comprises a sufficiently high concentration of gelatin, derived from human or animal tissue, such that prior to or upon implantation, the gelatin sets up to form a solid or semi-solid material of the desired shape.

4. The implant according to claim 3 further comprising cortical, cancellous or cortico-cancellous bone chips or demineralized bone.

5. The implant according to claim 4 wherein said bone chips are between about 125μm and about 5 mm in size.

6. The implant according to claim 5 wherein said bone chips are between about 500μm and about 1 mm in size.

7. The implant according to claim 5 wherein said bone chips are between about 1mm and 3.35 mm in size.

8. The implant according to claim 4 comprising, on a weight basis, a first component comprising: gelatin at between about 12 to 27 weight percent, demineralized bone at between about 15 to 33 weight percent, and the balance water, and a second component comprising: cortical bone chips, cancellous bone chips, or cortico-cancellous bone chips at a volume ratio of about 70 to 100 percent that of the combined gelatin/demineralized bone, said composition optionally including growth factors, antibiotics, anti-inflammatory or other biologically active agents.

9. The implant according to claim 1 comprising a disk shaped implant, a filled-C-shaped implant, a cone- or hemisphere-shaped implant, a U-shaped implant, a dowel or tapered-dowel shaped implant, donut-shaped implant, a filled-C-shaped implant having an asymmetric sector shaped space, a cup-shaped implant, a tube shaped implant, a sheet or strip-shaped implant, a cord-shaped implant, a wedge-shaped implant, a cork-shaped implant, a rib-shaped implant, a football-shaped implant, a hemi-football shaped implant, a sphere shaped implant, a hemi-sphere shaped implant, or an implant comprising an upper, cork-shaped segment, a seam and a lower hollow cone- or hemisphere-shaped segment.

10. The implant according to claim 1 when used in repair of an acetabular cup defect.

11. The implant according to claim 10 comprising a substantially disk-shaped device **100**, having an upper surface **101**, a lower surface **102**, each of which is substantially circular, with a diameter **110**, and a height **120.**

12. The implant according to claim 11 wherein the diameter **110** is in the range between about 35 and 55 mm.

13. The implant according to claim 12 wherein said diameter **110** is about 45 mm.

14. The implant according to claim 11 wherein said height **120** is in the range between about 1 mm and about 10 mm.

15. The implant according to claim 14 wherein said implant height **120** is about 5 mm.

16. The implant according to claim 11 wherein the disk **100** is composed of particulate matter, **130** embedded or suspended in a base or carrier material **140**.

17. The implant according to claim 16 wherein said particulate matter **130** is composed of collagen sponge, cortical bone chips, cancellous bone chips, cortico-cancellous bone chips, hydroxyapatite or like ceramics, bioactive glass, growth factors, bone morphogenetic protein, PDGF, TGFβ, vascular growth factors, demineralized bone, or combinations thereof.

18. The implant according to claim 17 wherein the base or carrier material **140** retains a given form upon implantation into a void space behind an acetabular implant.

19. The implant according to claim 18 wherein said carrier material **140** comprises fibrinogen, collagen, gelatin, hydroxylapatite, pleuronic polymers, natural or synthetic polymers, or carboxymethylcellulose, and combinations thereof.

20. The implant according to claim 1 comprising an upper surface **201**, a lower surface **202**, both of which are substantially circular, but wherein a sector **203** has been removed or has not been included in the formation of the device, resulting in a device having a "filled-C-shape", an angle **250**

formed between adjacent sides **204** and **205** that exist by virtue of the absent sector **203**, a diameter **210**, and a height **220.**

21. The implant according to claim 20 wherein the diameter **210** is between about 50 mm and about 150 mm.

22. The implant according to claim 21 wherein the diameter **210** is between about 75 mm and about 90 mm.

23. The implant according to claim 20 wherein the height **220** of the device is between about 1 mm and about 10 mm.

24. The implant according to claim 23 wherein said height **220** is about 5 mm.

25. The implant according to claim 20 comprising particulate material **230** composed of collagen sponge, cortical bone chips, cancellous bone chips, cortico-cancellous bone chips, hydroxyapatite or like ceramics, bioactive glass, growth factors, bone morphogenetic protein, TGFβ, PDGF, vascular growth factors, demineralized bone, and combinations thereof.

26. The implant according to claim 20 comprising a base or carrier material **140** which retains a given form upon implantation into a void space behind an acetabular implant.

27. The implant according to claim 26 wherein said carrier material **140** comprises fibrinogen, collagen, gelatin, hydroxylapatite, pleuronic polymers, natural or synthetic polymers, or carboxymethylcellulose, and combinations thereof.

28. The implant according to claim 20 wherein the angle **250** formed between the adjacent sides **204** and **205** is greater than 0 and less than 360 degrees.

29. The implant according to claim 28 wherein the angle **250** formed between the adjacent sides **204** and **205** is between about 90 degrees and 180 degrees.

30. The implant according to claim 29 wherein said angle **250** is about 120 degrees.

31. The implant according to claim 20 formed in the shape of a cone or hemisphere by bringing the adjacent sides **204** and **205** into contact.

32. The implant according to claim 1 comprising an implant selected from the group consisting of: a thin "U"-shaped implant **300** useful in knee revision or primary press-fit surgeries; a thicker "U"-shaped implant **310** useful in spinal fusion procedures; a thin oval implant **320** useful in knee revision or primary press-fit and other surgical procedures; an implant shape **330** useful in posterior lumbar interbody fusion ("PLIF") procedures; a dowel shaped implant **340**, useful in spinal and joint fusions; a tapered dowel shaped implant **350**, useful in spinal and joint fusions; a femoral or tibial ring shaped implant **400** useful in interbody fusion procedures; a round, plug-shaped implant **410** useful in cranial burr-hole repairs; a thin "U"-shaped implant **420** which may be folded to provide a cone- or hemisphere-shaped implant **430,** useful in knee replacement procedures; a thin implant **440** comprising a substantially circular shape and a void section, which may be folded onto itself to form a cone or hemisphere **450,** useful in acetabular cup reconstruction and other procedures; a substantially circular implant **510** comprising an asymmetric sector **511** which may be folded upon itself to form a cone or hemisphere **520,** useful in acetabular cup and like reconstructions; a "donut"-shaped implant **530** comprising a flat circular implant having a co-axial void, useful in acetabular cup reconstruction and like procedures where the implant is molded or press-fit to the void space; a hemi-shell shaped implant **540** which may be press-fit into a bone void, such as in the acetabular cup; a cone-or hemisphere-shaped implant **550** which may be press-fit into a bone void, such as in the acetabular cup; a tube **560** which, depending on

diameter, may be press-fit or used in an impaction grafting procedure in a bone intramedullary canal; a sheet **600** for repair of traumatic fractures, for cranial and flat-bone repair applications, and for inter-transverse process fusions; a strip **610** for repair of traumatic fractures, for cranial and flat-bone repair applications, and for inter-transverse process fusions; a cord-shaped implant **620** for wrapping or grouting of severe trauma defects, for spinal fusions, inter-transverse process fusions; a wedge-shaped implant **630** for tibial plateau repairs, joint fusions, and intervertebral body fusions; a restrictive devices, **640, 650, 700**, useful in restricting cement or other flowable materials in plugged intramedullary canals and the like, as in femoral canals during impaction procedures; an ovoid or football shaped implant **660** useful in repairing cystoid or like bone defects; a hemi-ovoid or hemi-football shaped implant **670** useful in repairing cystoid or like bone defects; a spherical implant **680** useful in repairing cystoid or like bone defects; and a hemi-spherical implant **690** useful in repairing cystoid or like bone defects.

33. The implant **650** according to claim 32 comprising a tapered, cork-like shape formed by a plurality of stacked "ribs" **651-655** of decreasing diameter.

34. The implant **700** according to claim 32 comprising an upper, solid portion **710** having a substantially "cork" shaped configuration, to which is affixed at seam **720** is a hollow, lower portion **730** which folds upward about seam **720** upon insertion of the implant **700** into a lumen **780** of a bone **790** to form a tight seal **740** surrounding the upper plug portion **710**.

35. A method of repairing a bone defect or void which comprises implanting therein an implant which exhibits the following characteristics:

a. the implant composition is bioabsorbable;

b. the implant composition is osteogenic;

c. the implant composition is ostcoinductive;

d. the implant composition is osteoconductive;

e. the implant composition is malleable prior to and shortly after implantation so that any desired shape may be produced to exactly conform to the shape of the implant site;

f. the implant composition is able to withstand freezing, freeze-drying, and sterilization; and

g. upon implantation, the implant material fills voids and then sets-up as a hard material in the shape of the voids that have been filled.

36. A method for inducing bone ingrowth into a porous implant or an implant comprising a porous coating which comprises contacting the surface of said implant with an implant according to claim 1.

37. A method for inducing bone ingrowth into an implant having multiple metal beads intended for contact with a cut bone surface which comprises contacting said metal beads of said implant with an implant according to claim1 such that said implant fills voids between said metal beads.

38. The method according to claim 37 wherein said implant is an implant used in total knee arthroplasty.

39. A method for making the implant according to claim 1, which comprises combining between one half to about an equal volume of a first composition comprising cortical bone chips, cancellous bone chips, or cortical-cancellous bone chips to a second component comprising gelatin, demineralized bone and water.

40. The method according to claim 39 which further comprises warming said combined first and second components, such that said combined components become intimately mixed and moldable, molding said combined components to form a desired shape, and cooling said combined and molded shape such that said combined components solidify in the form of said desired shape.

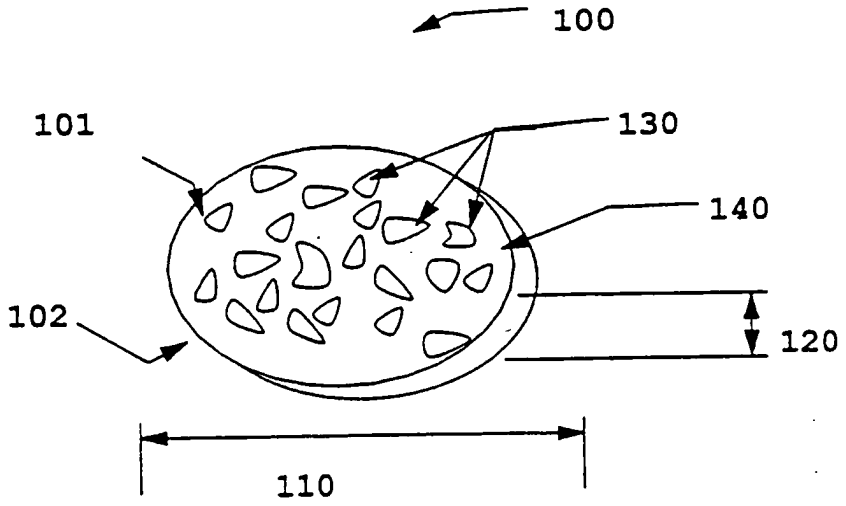

Figure 1

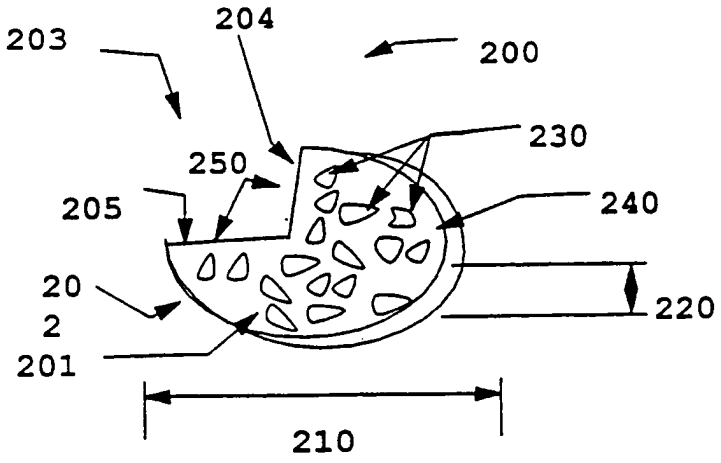

Fig. 2A

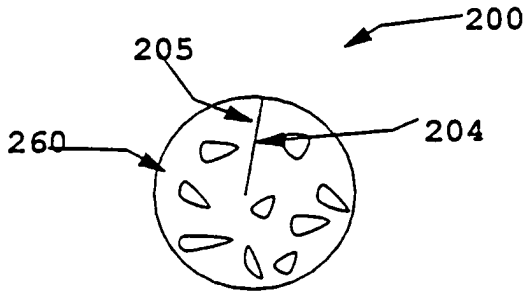

Fig. 2B

Figure 2

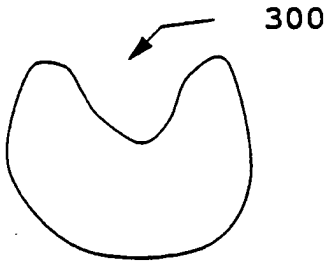

FIG. 3A

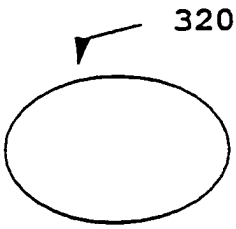

FIG. 3C

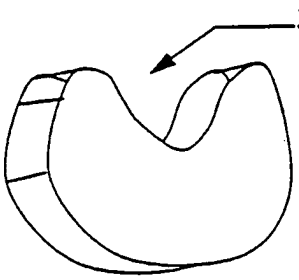

FIG. 3B

FIG. 3D

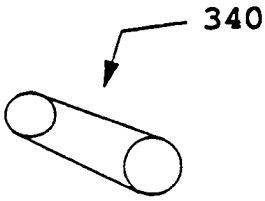

FIG. 3E

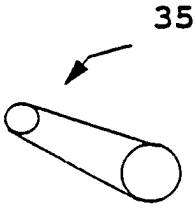

FIG. 3F

FIGURE 3

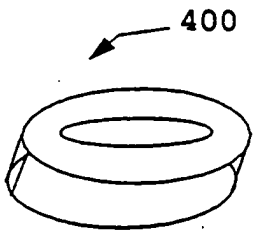

FIG. 4A

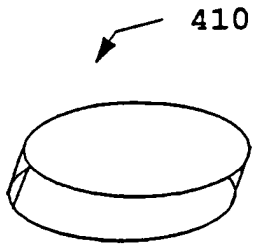

FIG. 4B

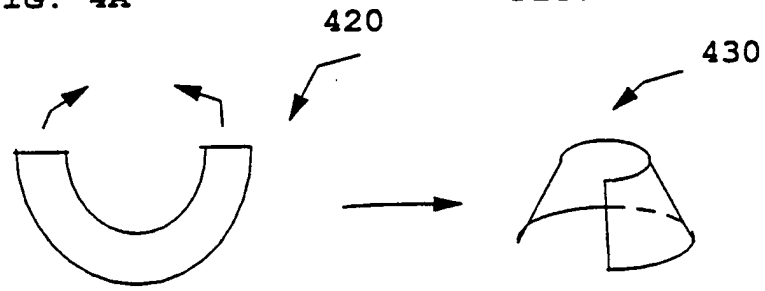

FIG. 4C

FIG. 4D

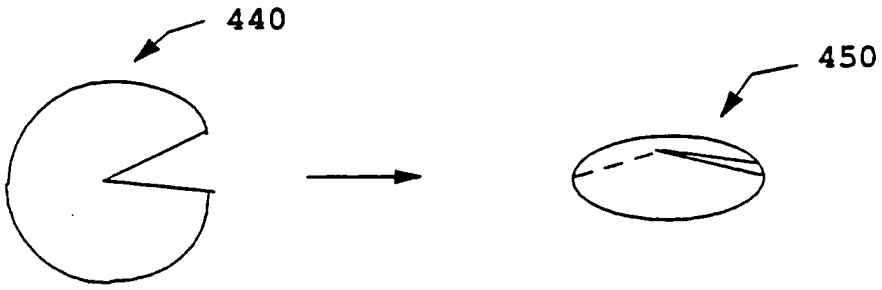

FIG. 4E

FIG. 4F

FIGURE 4

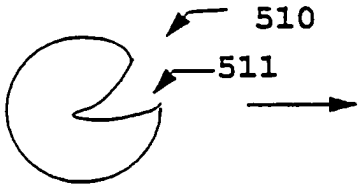

FIG. 5A

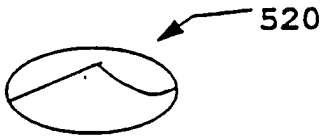

FIG. 5B

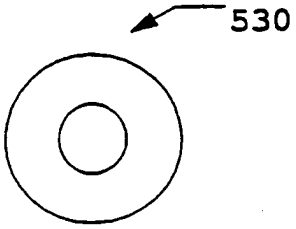

FIG. 5C

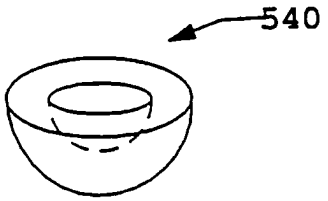

FIG. 5D

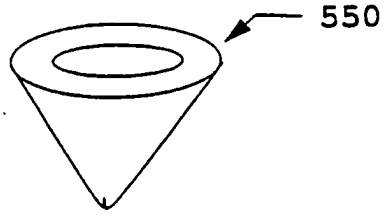

FIG. 5E

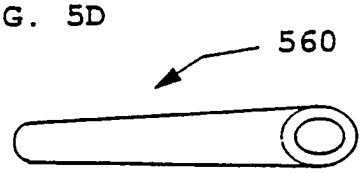

FIG. 5F

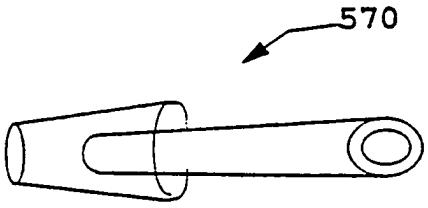

FIG. 5G

FIGURE 5

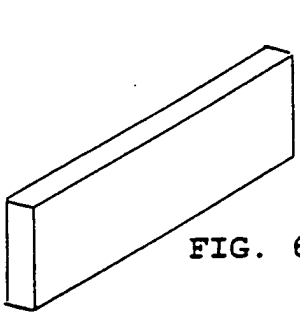

FIG. 6A

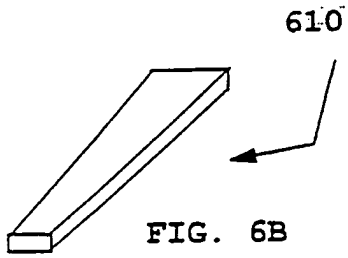

FIG. 6B

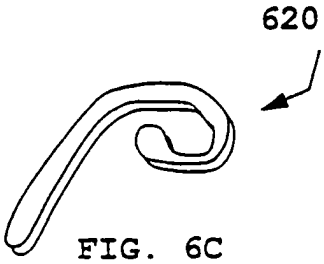

FIG. 6C

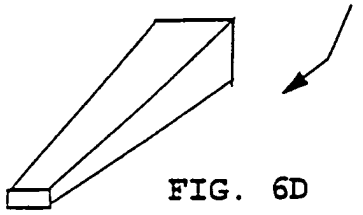

FIG. 6D

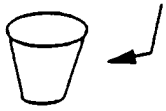

FIG. 6E

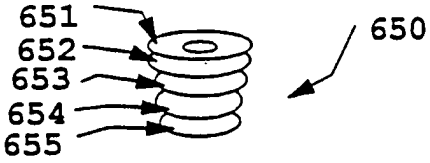

FIG. 6F

FIG. 6G

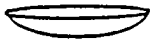

FIG. 6H

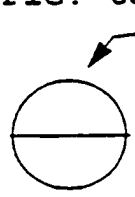

FIG. 6I

FIG. 6J

FIGURE 6

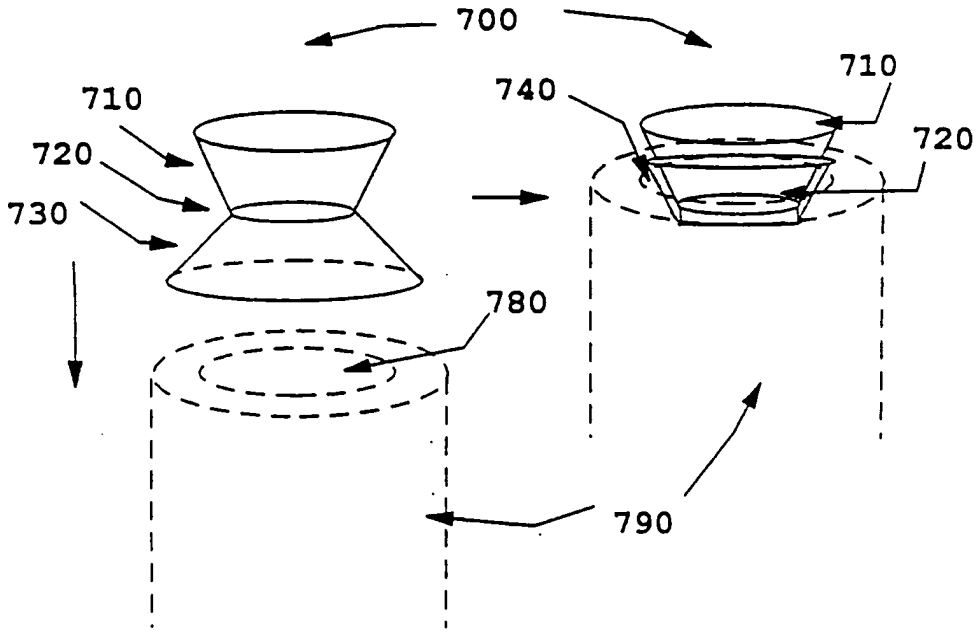

FIGURE 7

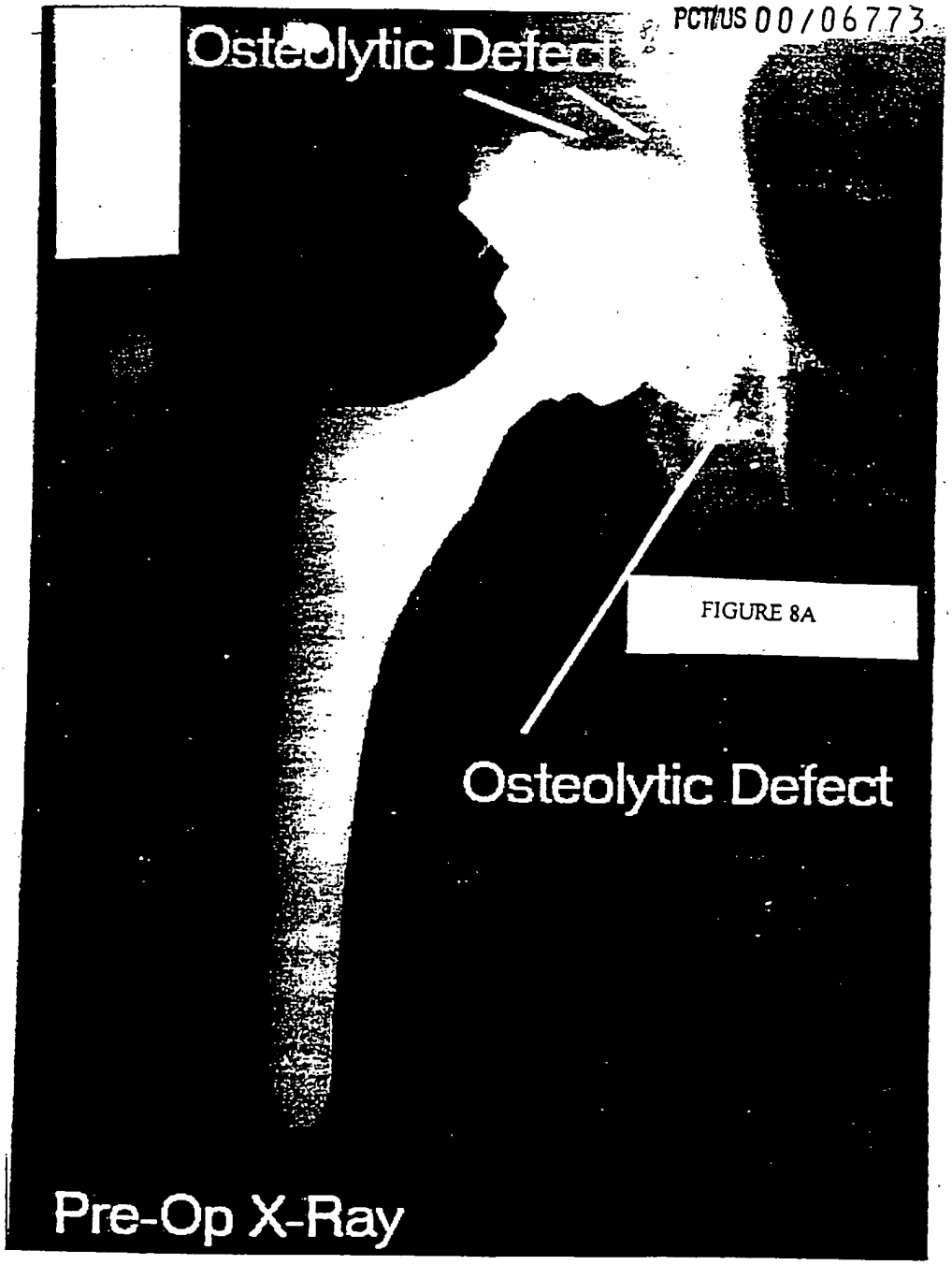
PCT/US 00/06773
Osteolytic Defect
Osteolytic Defect
Pre-Op X-Ray

FIGURE 8A

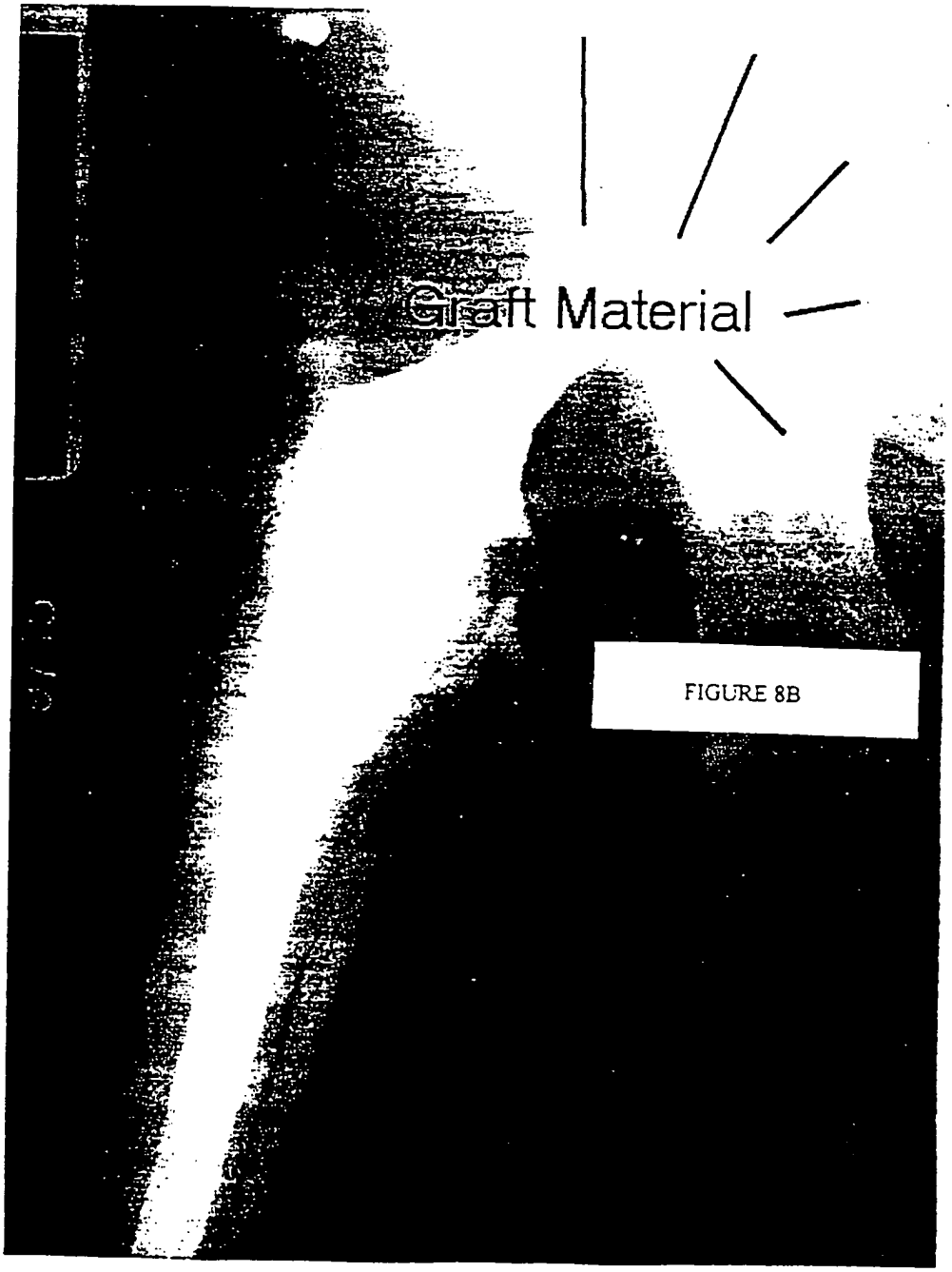

FIGURE 8B

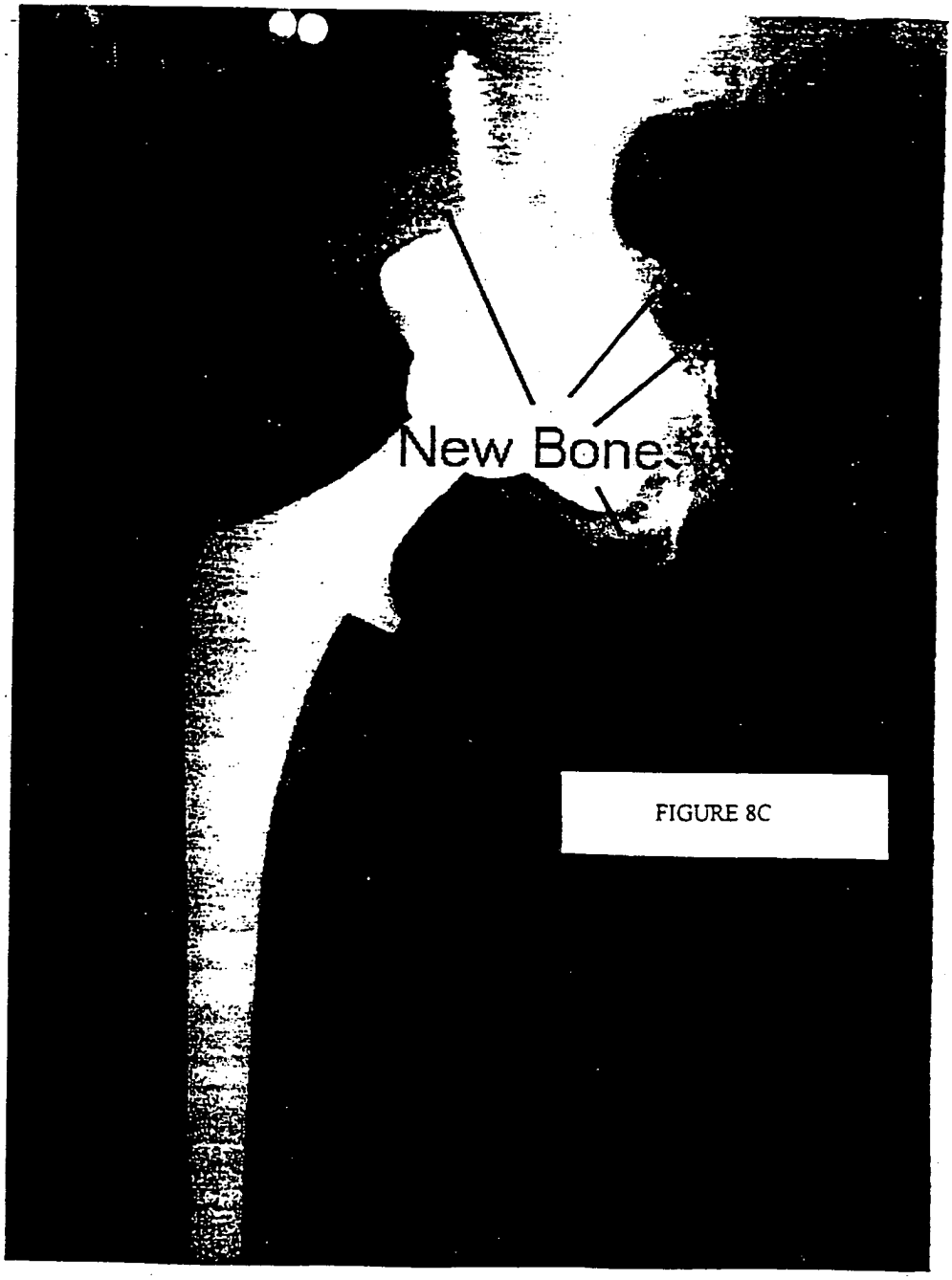

FIGURE 8C

FIGURE 9

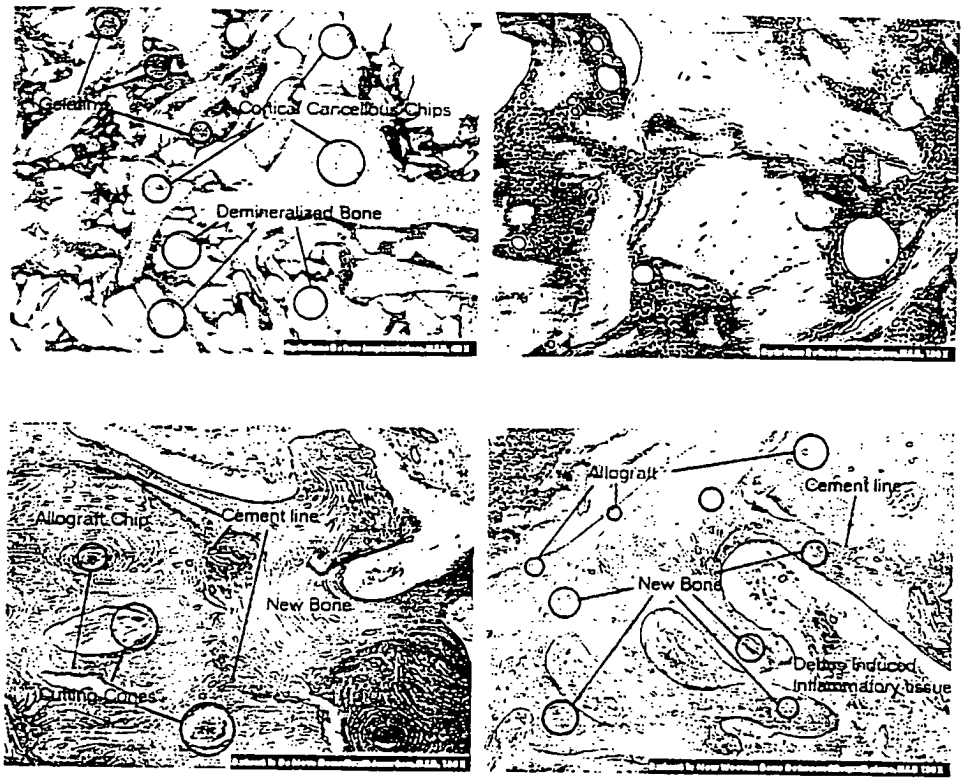
Gelatin
Cortical Cancellous Chips
Demineralized Bone
Allograft Chip
Cement line
New Bone
Cutting Cones
Allograft
Cement line
New Bone
Debris Induced Inflammatory Tissue

FIGURE 10

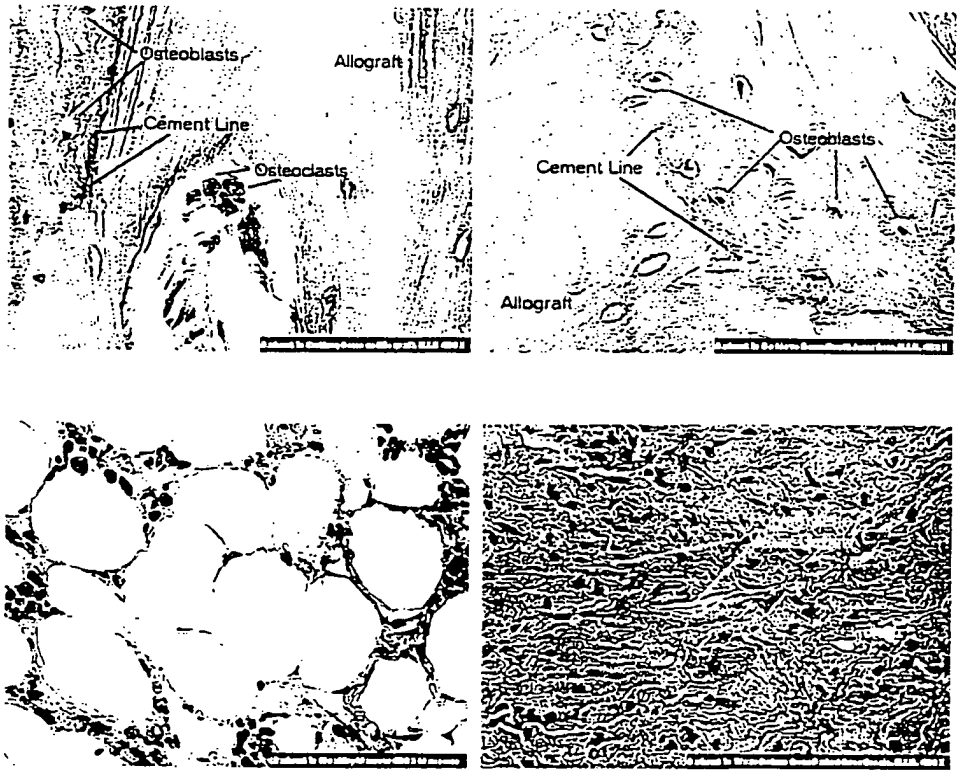
Osteoblasts
Allograft
Cement Line
Osteoclasts
Osteoblasts
Cement Line
Allograft

FIGURE 11A

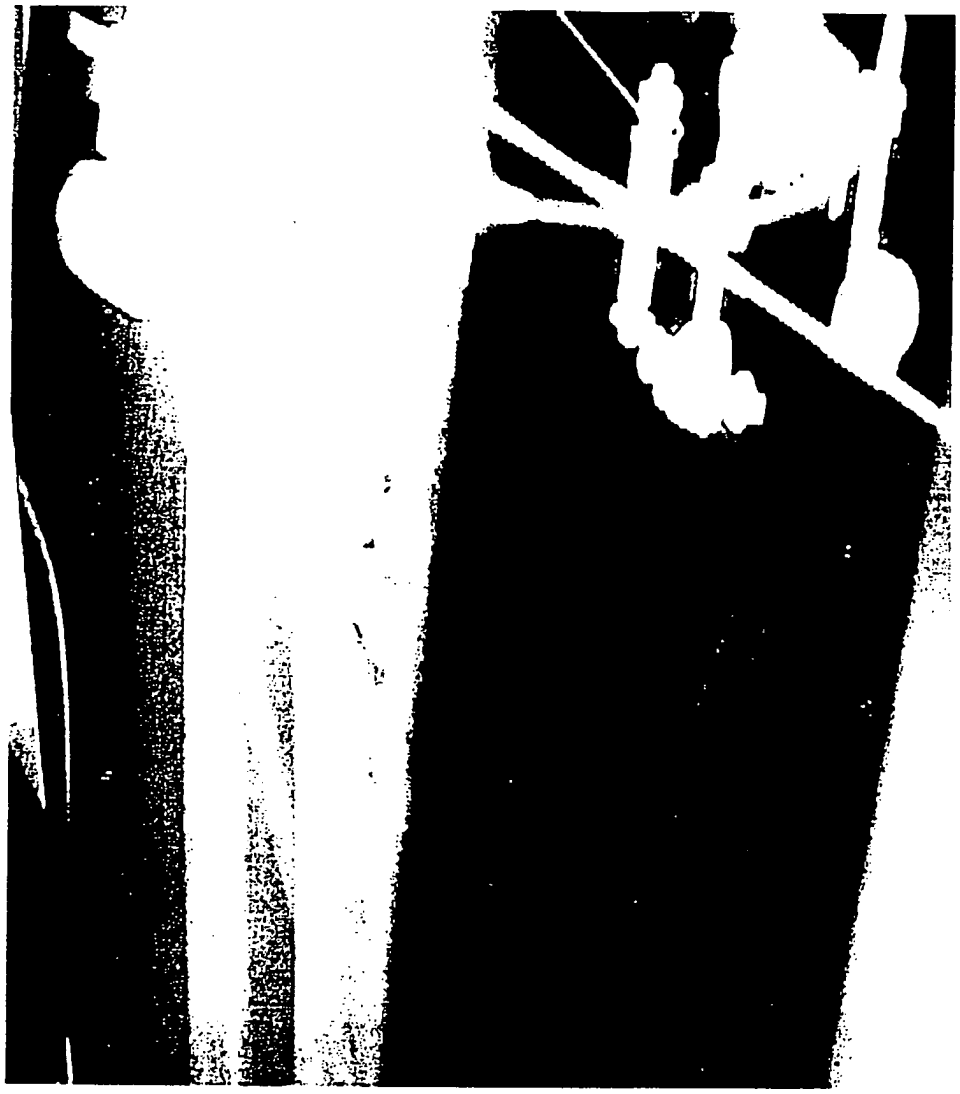

FIGURE 11B

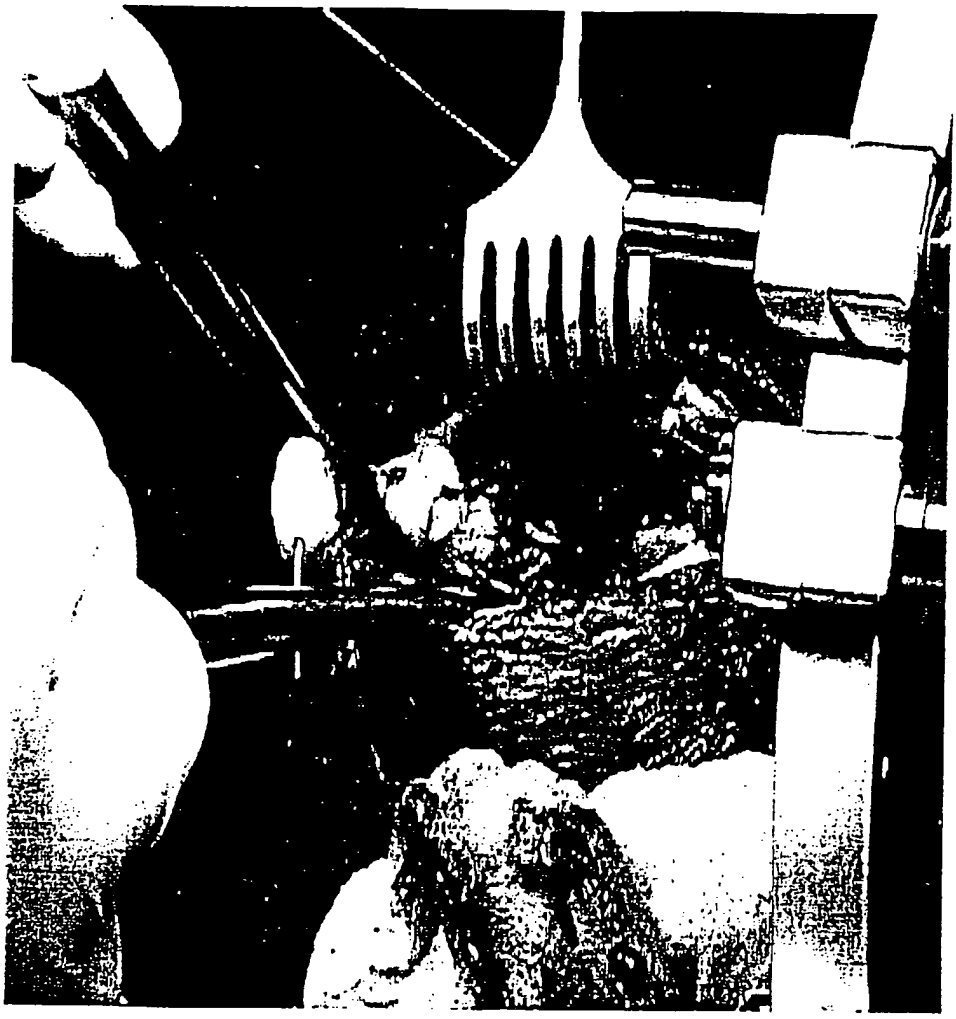

FIGURE 11C

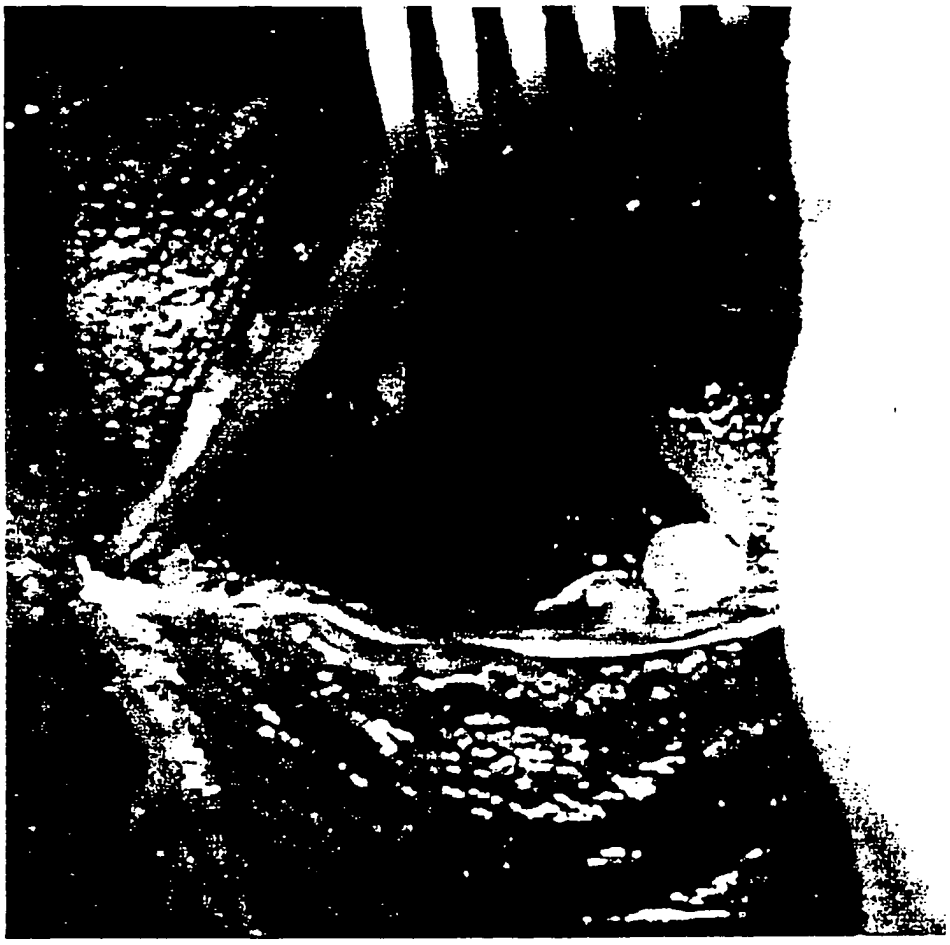

FIGURE 11D

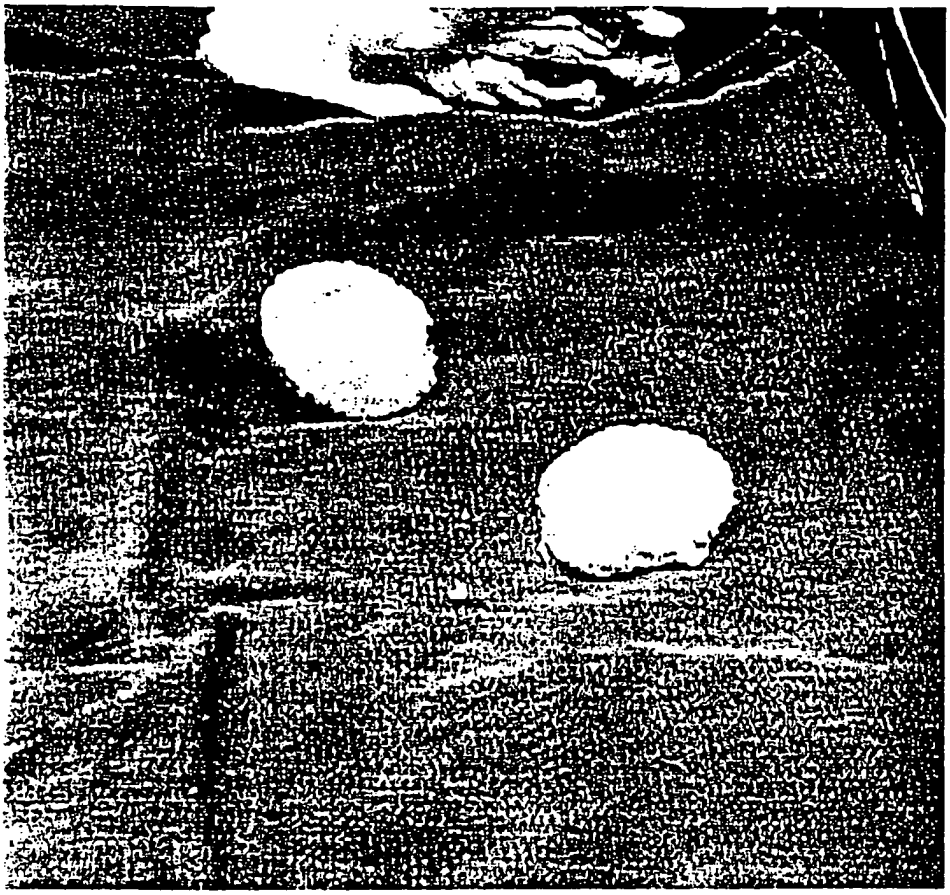

FIGURE 11E

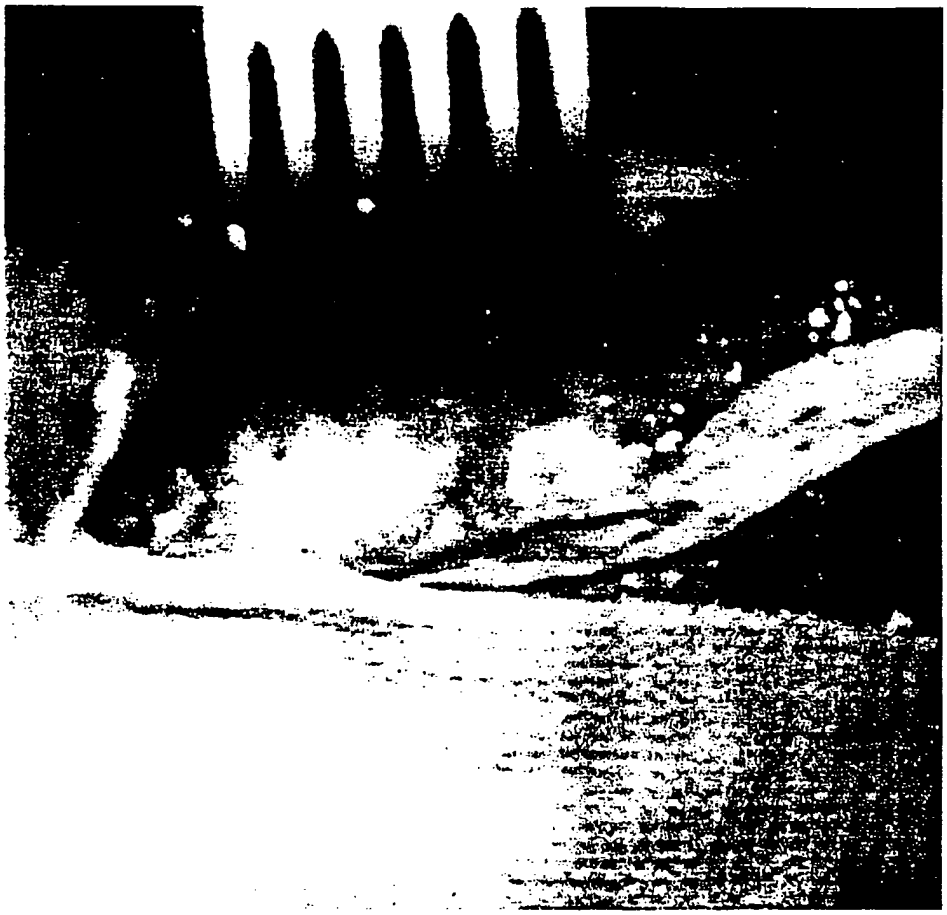

FIGURE 11F

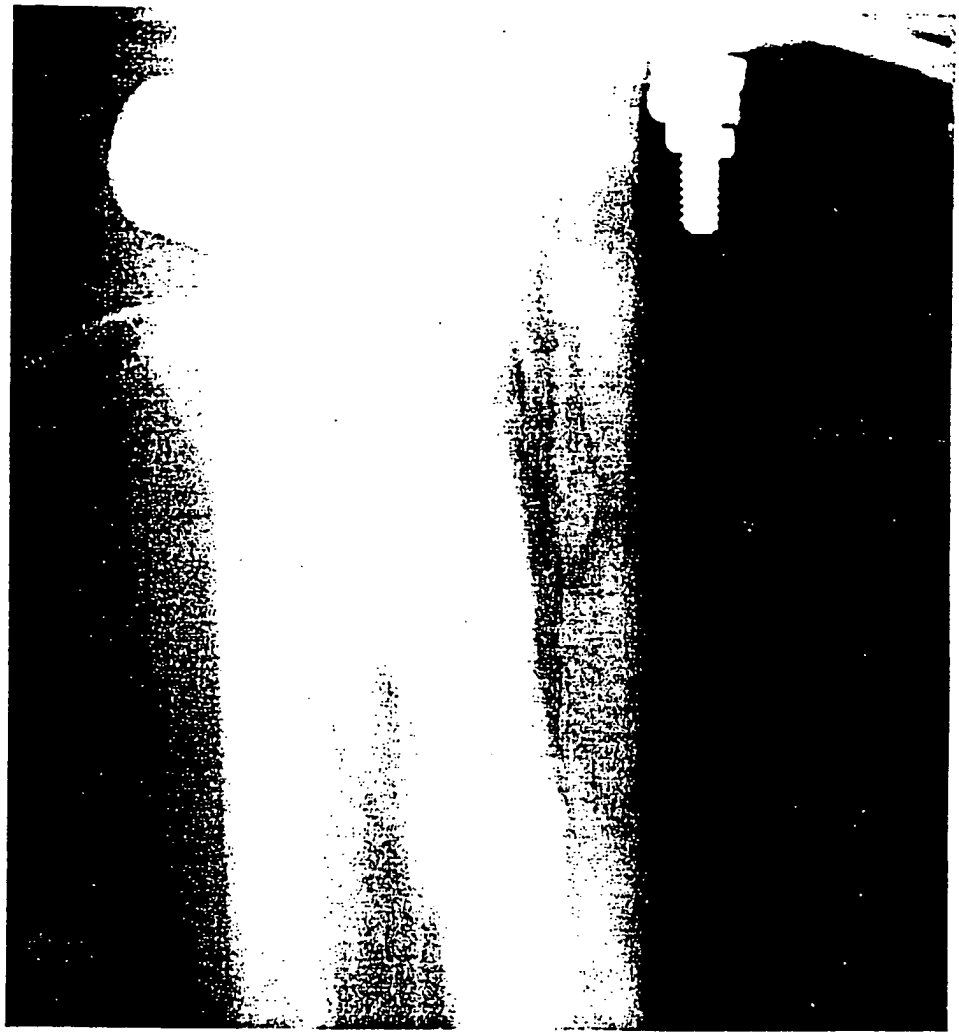

FIGURE 11G

FIGURE 11H

INTERNATIONAL SEARCH REPORT

Inter ional Application No
PCT/US 00/06773

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L25/00 A61L27/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	US 5 876 446 A (AGRAWAL C MAULI ET AL) 2 March 1999 (1999-03-02) the whole document	1-40
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A	WO 96 00592 A (UNIV TEXAS) 11 January 1996 (1996-01-11) the whole document	1-40

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
4 August 2000	17/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Korth, C-F

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INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 00/06773

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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Information on patent family members

Inter nal Application No
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